

RECEIVED
CENTRAL FAX CENTER

DOCKET NO.: CSKL0004-100

OCT 13 2006

PATENT

REMARKS

Claims 6 and 8-24 remain pending in the present application.

I. The Final Rejection is Premature

In the Office Action dated March 15, 2006, the Examiner rejected claims 6, 17, and 18 under 35 U.S.C. §103(a) over the Drenckhahn reference. Notably, claim 7 was *not* rejected under 35 U.S.C. §103(a) over the Drenckhahn reference. In the Amendment and Request for Reconsideration filed on May 18, 2006 in response thereto, Applicants amended claim 6 to incorporate the features of claim 7 which had not been rejected. Claim 6, which in essence is identical to original claim 7, is now under Final Rejection under 35 U.S.C. §103(a) over the same Drenckhahn reference. The Final Rejection presents the first rejection of claim 6 in its present form (essentially canceled claim 7). This rejection could have been made in the Office Action dated March 15, 2006, to which Applicants would have had an additional opportunity to respond. Thus, because the Final Rejection of claim 6 is premature, Applicants respectfully request that the Final Rejection be withdrawn.

II. The Claims Are Clear And Definite

Claims 1-6 and 8-22 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. As a preliminary matter, Applicants remind the Examiner that claims 1-5 were canceled on July 12, 2005 in response to the Restriction Requirement. Applicants traverse the rejection as is applied against claims 6 and 8-22 and respectfully request reconsideration because the claims are clear and definite.

The Office Action incorrectly asserts at page 2 that:

the claims are indefinite as to the ultimate objective of the method. The claims recite only process steps, and as such, virtually any objective would be encompassed.

The Office Action, however, fails to cite any legal support for the requirement of a descriptive preamble. As recognized by the Examiner, the claims recite process steps. The mere fact that "virtually any objective would be encompassed" has no bearing on whether the claims are

DOCKET NO.: CSKL0004-100

PATENT

indefinite. Indeed, persons of ordinary skill would have no difficulty in determining whether a particular process meets the features recited in the process steps recited in the claims. Accordingly, the claims are definite within the meaning of §112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims).

The Office Action also incorrectly asserts that the phrase “frozen second pyrene actin composition” in claim 9 “lacks *literal* antecedent basis” in claim 8 (emphasis added). There is absolutely NO requirement for “*literal* antecedent basis” in U.S. patent law. As set forth in MPEP 2173.05(e), “A claim is indefinite when it contains words or phrases whose meaning is unclear.” If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. *Ex parte Porter*, 25 USPQ.2d 1144 (Bd. Pat. App. & Inter. 1992). Step c) of claim 8 recites “rapidly freezing the second pyrene actin composition.” Claim 9, which is dependent on claim 8, quite clearly recites “lyophilizing the frozen second pyrene actin composition generated in step c.” Thus, the meaning of the phrase “frozen second pyrene actin composition” is quite clear. Indeed, the scope of claim 9 would be reasonably ascertainable by those skilled in the art. Further, the “frozen second pyrene actin composition” is an inherent feature once step c) of claim 8 is carried out. Requiring Applicants to recite “thereby generating a frozen second pyrene actin composition” in claim 8 would be an unreasonable and unwarranted application of U.S. patent law.

The Office Action also incorrectly asserts that the phrase “frozen second pyrene actin composition” in claim 12 “lacks *literal* antecedent basis” (emphasis added). Aside from the “literal” aspect again, claim 12 does not recite “frozen second pyrene actin composition.” Rather, claim 12 recites in its entirety “The process of claim 8, wherein the second pyrene actin composition is rapidly frozen in liquid nitrogen or a dry ice ethanol bath.”

The Office Action also incorrectly asserts that the phrase “frozen second pyrene actin composition” in claim 14 “lacks *literal* antecedent basis” (emphasis added). Notwithstanding the “literal” aspect again, claim 9, from which claim 14 depends, actually does provide even “literal” support for “frozen second pyrene actin composition.” The alleged lack of “literal antecedent basis” in the underlying claim 8 is referred to above.

DOCKET NO.: CSKL0004-100**PATENT**

In view of the foregoing, claims 6 and 8-22 are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

II. The Claimed Invention Is Not Obvious

A. The Drenckhahn Reference

Claims 6, 10, 11, and 15-19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Drenckhahn et al., J. Biol. Chem., 1986, 261, 12754 (hereinafter, the "Drenckhahn reference"). Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to modify the process set forth in the Drenckhahn reference to result in Applicants' claimed process.

The Drenckhahn reference reports that actin was purified from rabbit skeletal muscle using gel filtration. Part of the actin was labeled with pyrene iodoacetamide (to create pyrene actin) and used at 1-5% of the total actin in a fluorescence assay for polymerized actin. The polymerization assay was carried out in standard buffer which included KCl, MgCl₂, EGTA, dithiothreitol, CaCl₂, ATP, and imidazole. The Drenckhahn reference does not teach a step of concentrating the pyrene actin composition prior to mixing with sucrose, a stabilizing agent, and a reducing agent.

The Office Action recognizes that the Drenckhahn reference does not teach a step of concentrating the pyrene actin composition (see page 3 of the Office Action). The Office Action, however, asserts that "the process of preparing the pyrene actin would result in a dilute solution of the target material" and that "one of ordinary skill would have been motivated to increase the concentration of the pyrene actin to a point where only small volumes of the solution would be required for the subsequent assay." The Examiner provides no basis or evidence for these assertions. Indeed, the Examiner provides no support for the assertion that the process of preparing the pyrene actin would result in a solution that was too dilute to use in the polymerization assay. Indeed, as recognized by the Examiner, the authors of the Drenckhahn reference (presumably they are considered to be skilled in the art) did not teach concentration of the pyrene actin prior to its use in the polymerization assay. Thus, the pyrene actin composition was apparently in a state that was suitable for use in the polymerization assay. Further, the

DOCKET NO.: CSKL0004-100

PATENT

pyrene actin was used at 1-5% of the total actin in the polymerization assay. One skilled in the art would not have been motivated to concentrate the pyrene actin just prior to diluting it again with 20-times to 99-times the amount of unlabeled actin.

The Office Action also asserts that "it is more convenient to store a small volume of concentrated solution than to store a large volume of a dilute solution." There is no indication that the authors of the Drenckhahn reference were seeking to store anything. Indeed, they were using the pyrene actin in the polymerization assays. Further, this level of motivation is not sufficient. In establishing a *prima facie* case of obviousness under 35 U.S.C. §103, it is incumbent upon the Examiner to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. *Ex parte Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). To this end, the requisite motivation must stem from some teaching, suggestion or inference in the prior art as a whole or from the knowledge generally available to one of ordinary skill in the art and not from appellants' disclosure, see for example, *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988); and *Ex parte Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Pat. App. Int. 1992). In this respect, the following quotation from *Ex parte Levengood*, 28 U.S.P.Q.2d 1300, 1302 (Pat. Off. Bd. App. 1993), is noteworthy:

Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a *prima facie* case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that "would lead" that individual "to combine the relevant teachings of the references." ... Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force that would **impel** one skilled in the art to do what the patent applicant has done. (citations omitted; emphasis added)

Significantly, the Office Action identifies no "motivating force" that would "impel" persons of ordinary skill to modify the teachings of the Drenckhahn reference and achieve the claimed invention.

DOCKET NO.: CSKL0004-100

PATENT

Thus, there is no motivation to modify the process set forth in the Drenckhahn reference to incorporate a concentration step. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

B. The Combination of the Drenckhahn and Pollard References

Claims 6, 10, 11, and 15-19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Drenckhahn et al., J. Biol. Chem., 1986, 261, 12754 (hereinafter, the "Drenckhahn reference") in view of Pollard, J. Cell Biol., 1984, 99, 769 (hereinafter, the "Pollard reference"). Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to modify the process set forth in the Drenckhahn reference by the teachings of the Pollard reference to produce Applicants' claimed process, and even if combined, the references do not produce Applicants' claimed invention.

The Pollard reference reports a process of actin purification whereby actin was purified from *Acanthamoeba castellanii* and subsequently chromatographed on DEAE-cellulose. The actin was then polymerized and pelleted by centrifugation. The pellets were homogenized in a buffer and dialyzed against several changes of the buffer over 2-3 days. After clarification by centrifugation, the actin was polymerized. After pelleting and depolymerizing, purification was completed by gel permeation chromatography. The remainder of the clarified, once-polymerized actin was polymerized and labeled with pyrene-iodoacetamide using a 7:1 ratio of dye to actin and mixing slowly for 5-18 hours. After pelleting and depolymerization, the pyrene-actin was purified by chromatography on G-150. The pyrene-actin was then mixed with unlabeled actin.

The Office Action asserts that the Pollard reference is cited "because Drenckhahn refers to it [citation omitted] as the process which was used to make the pyrene actin." The Office Action further states that the Pollard reference reports a "procedure in which the pyrene actin is pelleted" and that this pelleting is a form of concentration. The Examiner, however, has misunderstood the teachings of the Pollard reference. Indeed, the Pollard reference teaches that the "remainder of the clarified, once-polymerized actin was polymerized and labeled with pyrene-iodoacetamide using a 7:1 ratio of dye to actin and mixing slowly for 5-18 hours." The Pollard reference then teaches that "after pelleting *and depolymerization*, the pyrene-actin was purified by chromatography on G-150" prior to mixing with unlabeled actin (emphasis added).

DOCKET NO.: CSKL0004-100**PATENT**

The act of pelleting creates concentrated polymers of actin. Thus, prior to mixing with unlabeled actin, the pyrene actin was again depolymerized (i.e., homogenizing the pellets in a buffer and dialyzed against several changes of the buffer over 2-3 days). Thus, the combination of the Drenckhahn reference with the Pollard reference results in preparation of pyrene actin, pelleting of the pyrene actin, depolymerizing the pyrene actin, purifying the pyrene actin by chromatography and mixing the pyrene actin with unlabeled actin in the polymerization assay. In contrast, claim 6 recites a process comprising concentrating a pyrene actin composition, and mixing the concentrated pyrene actin composition with sucrose, a stabilizing agent, and a reducing agent, thereby generating a second pyrene actin composition. Although the Pollard reference reports pelleting pyrene actin, it also reports depolymerizing the pyrene actin prior to mixing with unlabeled actin. Depolymerization is the opposite of pelleting. The Office Action cannot simply focus on one particular element of the Pollard reference while ignoring other teachings of the reference as a whole. Thus, there is no motivation to modify the process set forth in the Drenckhahn reference with the pelleting element found in the Pollard reference. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

C. The Combination of the Drenckhahn and Cooper References

Claims 6, 10, 11, and 15-19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the Drenckhahn reference in view of Cooper, J. Musc. Res. Cell Motil., 1983, 4, 253 (hereinafter, the "Cooper reference"). Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to modify the process set forth in the Drenckhahn reference by the teachings of the Cooper reference to produce Applicants' claimed process, and even if combined, the references do not produce Applicants' claimed invention.

The Cooper reference reports a process of actin purification whereby after purification, 7.5 mol of N-(1-pyrenyl)iodoacetamide were added per mol of actin. The mixture was rotated for 16 to 24 hours prior to collection of the actin filaments by centrifugation. The pellet was then homogenized in a buffer and the mixture dialyzed against the buffer for 48 hours. After clarification by centrifugation, the upper $\frac{3}{4}$ of the supernatant was chromatographed on Sephadex G-150 to yield monomeric pyrene-labelled actin.

DOCKET NO.: CSKL0004-100**PATENT**

The Office Action asserts that the Cooper reference is cited because the Drenckhahn reference cites the Pollard reference which in turn cites the Cooper reference. No evidence, let alone any analysis, is provided in the Office Action. No motivation for the combination of the cited references is even provided in the Office Action. The combination of the Drenckhahn reference with the Cooper reference results in preparation of pyrene actin, pelleting of the pyrene actin by centrifugation, depolymerizing the pyrene actin by homogenizing the pellet in a buffer, centrifuging the homogenized pyrene actin, purifying the pyrene actin by taking a portion of the supernatant and subjecting it to chromatography, and then mixing the pyrene actin with unlabeled actin in the polymerization assay. In contrast, claim 6 recites a process comprising concentrating a pyrene actin composition, and mixing the concentrated pyrene actin composition with sucrose, a stabilizing agent, and a reducing agent, thereby generating a second pyrene actin composition. Although the Cooper reference, like the Pollard reference, reports pelleting pyrene actin, it also reports depolymerizing the pyrene actin. Again, depolymerization is the opposite of pelleting. Likewise to the analysis of the combination of the Drenckhahn and Pollard references discussed above, the Office Action cannot simply focus (to the extent it focused on anything) on one particular element of the Cooper reference while ignoring other teachings of the reference as a whole. Thus, there is no motivation to modify the process set forth in the Drenckhahn reference with the pelleting element found in the Cooper reference. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

D. The Combination of the Drenckhahn and Blatt or Cordle References

Claims 6, 10, 11, and 15-19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the Drenckhahn reference in view of either Blatt, Amer. Lab., 1969, March, 21 (hereinafter, the "Blatt reference") or U.S. Patent No. 4,897,465. Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to modify the process set forth in the Drenckhahn reference by the teachings of either the Blatt reference or the Cordle reference to produce Applicants' claimed process.

The Blatt and Cordle references report general methods of concentrating protein-containing mixtures using ultrafiltration. Neither reference teaches or even suggests concentrating a pyrene actin concentration.

RECEIVED
CENTRAL FAX CENTER

DOCKET NO.: CSKL0004-100

OCT 13 2006

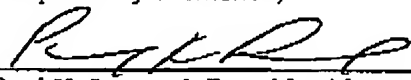
PATENT

The Office Action asserts that while the Drenckhahn reference does not teach that when one is in possession of a dilute pyrene actin composition, that "benefit may accrue to the practitioner upon concentrating the composition," one of ordinary skill would have been motivated to increase the concentration of a dilute solution of pyrene actin such as by means reported in the secondary references (see page 5 of the Office Action). Again, the Office Action fails to provide any reasoning, let alone evidence to support the assertion that one skilled in the art would be motivated to increase the concentration of a dilute solution of pyrene actin. Indeed, as explained above, the solution of pyrene actin obtained by the authors of the Drenckhahn reference was apparently of sufficient dilution to use (and, in fact, is further diluted when added to the unlabeled actin) in the polymerization assay. The only motivation for concentrating the pyrene actin prior to mixing with sucrose, a stabilizing agent, and a reducing agent comes from Applicants' specification. Thus, there is no motivation to modify the process set forth in the Drenckhahn reference with the ultrafiltration methods reported in either of the Blatt or Cordle references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

III. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 665-6914 if there are any questions regarding Applicants' claimed invention. Applicants also request an interview if a Notice of Allowance is not forthcoming.

Respectfully submitted,


Paul K. Legaard, Reg. No. 38,534

Date: 13 October 2006
COZEN O'CONNOR, P.C.
1900 Market Street
Philadelphia, PA 19103-3508
Telephone: (215) 665-6914
Facsimile: (215) 701-2141